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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,507	11/22/2000	Joseph A. Affholter	02-104244US	5232
30560	7590	07/29/2004	EXAMINER	
MAXYGEN, INC. INTELLECTUAL PROPERTY DEPARTMENT 515 GALVESTON DRIVE RED WOOD CITY, CA 94063			JOHANNSEN, DIANA B	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,507	AFFHOLTER ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 02 April 2004.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 120-157 is/are pending in the application.
- 4a) Of the above claim(s) 130,131 and 142-153 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 120-129,132-141 and 154-157 is/are rejected.
- 7) Claim(s) 120-129,132-141 and 154-157 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 22 November 2000 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>0101a, 0101b, 0601</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Election/Restriction

1. Applicant's election of the species of an enzymatic activity or property for a), a semi-aqueous system for b), and a ligase for c) in the reply filed on April 2, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 130-131 and 142-153 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected election, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 2, 2004. It is noted that while Applicant has identified claim 130 as one of the claims readable on the elected species, claim 130 recites a variety of screening conditions but does not include that elected by Applicant (applicant elected a "semi-aqueous system" as recited in claim 132). See page 2 of the Election/Restriction of October 2, 2003 for a list of all of the screening conditions of b).

Information Disclosure Statement

3. The information disclosure statement filed January 11, 2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Accordingly, only cited U.S. Patents and publications for which copies were provided (either in the instant application or in parent application 09/656,549) have been considered.

Specification

4. The specification fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 because the specification recites sequences that lack description by the appropriate sequence identifier set forth in the "Sequence Listing" as required by 37 CFR § 1.821(d). See, for example, Figures 6-8, and the descriptions thereof: neither the Figures nor their descriptions provide the SEQ ID NOs for the sequences recited therein. Appropriate corrections for compliance are required. With respect to figures/descriptions lacking the necessary SEQ ID Nos, it is noted Applicant may either file substitute Figures that recite the appropriate sequence identifiers, or amend the brief description of the figures so as to set forth said sequence identifiers. See MPEP 2422.02.

5. The use of numerous trademarks has been noted in this application.

Trademarks should be capitalized wherever they appear.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Objections

6. Claims 120-129, 132-141, and 154-157 are objected to because of the following informalities: in the second line of claim 120, "two" is misspelled "to" (in the phrase "wherein a first of the at least to sets..."). Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 120-129, 132-141, and 154-157 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 120-129, 132-141, and 154-157 are indefinite over the recitation of the limitation "wherein hybridization of the first and second sets of nucleic acids directs combinatorial assembly of a third set of nucleic acids" in claim 120. First, while the claims are drawn to a method of "combinatorially assembling nucleic acids," the recitation "wherein hybridization....third set of nucleic acids" does not appear to require that "combinatorial assembly" actually take place during the practice of the claimed method (rather, it appears that hybridization may, e.g., "direct" assembly at some other time). Second, it is not clear from this language whether hybridization products formed during the "hybridizing" step of the method themselves constitute a combinatorially assembled "third set of nucleic acids," or whether, e.g., some further action or structural modification is required to produce a set of nucleic acids that would be considered a combinatorially assembled "third set" meeting the claims. Clarification is required.

Claims 123-124 are indefinite over the recitation of the limitation "the cell" in each of the claims because there is insufficient antecedent basis for this limitation.

Claim 125 is indefinite over the recitation of the limitation "wherein the first or second set of nucleic acids are homologous." The term homologous refers to a relationship between two or more molecules; for example, a first molecule that shares homology with a second molecule may be described as "homologous" to the second

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molecule. However, in the instant case, the claim does not indicate with what or to what the first or second set is homologous. For example, does this recitation refer to a relationship amongst the first or second set of molecules (e.g., such that all members of the first set are homologous to each other), or does the recitation require that a set be homologous to a particular molecule? Clarification is required.

Claim 129 is indefinite over the recitation of the limitation “the trait or property” because there is insufficient antecedent basis for this limitation.

Claims 138 and 140-141 are indefinite over the recitation of the limitation “wherein the combinatorial assembly comprises at least one nucleic acid ligase” in claim 138. It is unclear whether the recitation requires that the claimed method employ a nucleic acid ligase, or whether the recitation requires that the resulting “combinatorial assembly” product include a ligase. Clarification is required.

Claim 156 is indefinite over the recitation “further comprising a logical cataloging step.” First, this language does not indicate what is to be “logically cataloged.” Second, as neither the specification nor the art provide a clear, limiting definition for the term “logical cataloging,” it is not clear how this recitation further limits the claims (i.e., what actual actions or manipulations would be required in order for one to have performed “logical cataloging”?). Clarification is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 120-129, 132-133, 137-141, and 155-156 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Vind (WO 98/41653 [published 24 September 1998]).

Vind discloses methods for preparing a “library of recombinant homologous polynucleotides” comprising steps of hybridizing primers to single stranded DNA templates (followed by primer extension), as well as optional steps of employing extended primers as both primers and templates in further steps of hybridization and extension (see entire reference, particularly pages 5-6, 11-12). It is an inherent property of the method of Vind that it is a method of and results in the production of “combinatorially assembled nucleic acids,” as required by the instant claims. Further, it is an inherent property of both the single-stranded templates and denatured primer extension products of Vind that they meet the requirements of the “first set” of nucleic acids of the claimed method, and of both the primers and denatured primer extension products of Vind that they meet the requirements of the “second set” of nucleic acids of the claimed method. With further regard to claim 122 and 133, Vind discloses cloning and transformation of hybridization products, such that the “third set of nucleic acids” is contained in cells (see, e.g., pages 7, 15). With respect to claims 123, 126 and 139, it is noted that the method of Vind employs polymerase in extension steps, and that the

polymerases disclosed by Vind for use in his method include “engineered or mutant” polymerases (see, e.g., pages 6, 11-12). Further, with regard to the elected invention (comprising the use of a ligase; see claims 123, 126, 138, and 140-141), Vind also discloses the use in his method of ligase it is noted that Vind discloses the use of ligase in a ligation step prior to transformation/transduction, including the use of T4 DNA ligase (see pages 26, 29). Regarding claim 125, Vind discloses the use of a population of homologous template molecules in his methods (see, e.g., pages 5-6; 23). Regarding claim 127, it is an inherent property of the method of Vind that it produces a variety of template and primer hybrids, which molecules are overlapping with respect to one another. Regarding claims 128-129 and 132, Vind discloses expression and screening of novel hybrid polypeptides, including a variety of enzymes with “improved” properties, and further discloses selection/screening in a “semi-aqueous” system (e.g., a system employing both liquid and solids [filters] and/or semi-solids [gel materials, agar, etc.]) (see, e.g., pages 7-8, 15, 20-21). With respect to claims 155-156, Vind exemplifies sequencing of the “third set” of nucleic acids (see, e.g., pages 26, 29), and further exemplifies a “logical cataloging” step (specifically of sorting products into different categories, as disclosed at pages 27 and 30).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claim 134 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vind (WO 98/41653 [published 24 September 1998]) in view of Resnick (U.S. Patent No. 5,807,724 [published 15 September 1998]).

Vind discloses methods for preparing a "library of recombined homologous polynucleotides" comprising steps of hybridizing primers to single stranded DNA templates (followed by primer extension), as well as optional steps of employing extended primers as both primers and templates in further steps of hybridization and extension (see entire reference, particularly pages 5-6, 11-12). It is a property of the method of Vind that it is a method of and results in the production of "combinatorially assembled nucleic acids," as required by the instant claims. Further, it is a property of both the single-stranded templates and denatured primer extension products of Vind that they meet the requirements of the "first set" of nucleic acids of the claimed method, and of both the primers and denatured primer extension products of Vind that they meet the requirements of the "second set" of nucleic acids of the claimed method. Vind also

discloses expression and screening of novel hybrid polypeptides, including a variety of hybrid enzymes with "improved" properties, and further discloses selection/screening in a "semi-aqueous" system (e.g., a system employing both liquid and solids [filters] and/or semi-solids [gel materials, agar, etc.]) (see, e.g., pages 7-8, 15, 20-21). It is further noted that Vind discloses and exemplifies the preparation of hybrid lipases (see, e.g., pages 11, 20; Examples 1-2). However, Vind does not disclose a semi-aqueous screening system comprising "crude oil or distillation fractions derived therefrom" as required by claim 134. Resnick discloses particular lipases that are effective at breaking down "crude oil and other petroleum distillates" (see entire reference, particularly column 1, line 52-column 2, line 5), and further discloses that such lipases are useful in "remediation of chemical and petrochemical spills" (see entire reference, particularly column 1, lines 13-19). In view of the teachings of Resnick, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Vind so as to have employed therein the particular lipases of Resnick, and so as to have screened the recombinant polypeptides produced by said method in a semi-aqueous system comprising crude oil or other petroleum distillates for an improved ability to degrade such oil or distillates. An ordinary artisan would have been motivated to have made such a modification in order to have identified novel hybrid lipases with an improved ability to degrade oil or oil distillates, for the advantage of providing for improved remediation of crude oil spills.

15. Claims 135-136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vind in view of Resnick, as applied to claim 134, above, and further in view of Monticello et al (U.S. Patent No. 5,358,870 [25 October 1994]).

The combined teachings of Vind and Resnick do not teach the screening of novel hybrid enzymes for “an appearance or disappearance of organic or inorganic sulfur” (claim 135) or for a “rate or an extent of substrate desulfurization” (claim 136). Monticello et al disclose the use of enzymes that cleave carbon-sulfur bonds in the desulfurization of petroleum liquids (see entire reference). Monticello et al further disclose a variety of methods for monitoring the disappearance of sulfur, including the rate and extent of desulfurization (see, e.g., column 13, line 7-column 14, line 12). In view of the teachings of Monticello et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Vind and Resnick so as to have screened for the disappearance of sulfur from crude oil, as well as for the rate and/or extent of desulfurization. An ordinary artisan would have been motivated to have made such a modification for the advantage of identifying novel hybrid enzymes having the additional capability of performing desulfurization of crude oil.

16. Claims 154 and 157 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vind in view of Christians et al (Nature Biotechnology 17:259-264 [3/1999]).

Vind discloses methods for preparing a “library of recombinant homologous polynucleotides” comprising steps of hybridizing primers to single stranded DNA templates (followed by primer extension), as well as optional steps of employing

extended primers as both primers and templates in further steps of hybridization and extension (see entire reference, particularly pages 5-6, 11-12). It is a property of the method of Vind that it is a method of and results in the production of "combinatorially assembled nucleic acids," as required by the instant claims. Further, it is a property of both the single-stranded templates and denatured primer extension products of Vind that they meet the requirements of the "first set" of nucleic acids of the claimed method, and of both the primers and denatured primer extension products of Vind that they meet the requirements of the "second set" of nucleic acids of the claimed method. Vind does not disclose the use of "a robotic arm, a robotic platform, or another computer-controlled electromechanical device," as required by claim 154. Further, Vind does not teach a further step of "displaying one or more members of the third set nucleic acids or expression products thereof in an array," as set forth in claim 157. Christians et al disclose the use of a robot to prepare and screen large numbers of novel chimeric enzymes, as well as the preparation of an array of hybrids to be screened on nylon filters (see entire reference, particularly page 263, right column). In view of the teachings of Christians et al, it would have been *prima facie* obvious to one of ordinary skill in the art to have modified the method of Vind so as to have employed robotic technology in the preparation and screening of novel chimeric molecules, as well as arrays in screening of those molecules. An ordinary artisan would have been motivated to have made such a modification in order to have performed the method of Vind in a more rapid, high-throughput manner, for the advantages of increased efficiency and speed in practicing Vind's method.

Drawings

17. The drawings are objected to because Figures 4-5 have inadequate top margins. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Diana B. Johannsen
Primary Examiner
July 22, 2004